

### **REMARKS**

Claims 18-20 have been added. No new matter has been introduced by virtue of those new claims. For instance, support for the new claims appears e.g. in the original claims of the application.

Claims 7-10 and 12-17 were rejected under 35 U.S.C. §103(a) over Sasse, et al., The Journal of Antibiotics, 2000, 53, 879-885, in view of Greenwald, Journal of Controlled Release, 2001, 74, 159-171.

As set forth at pages 2-3 of the Office Action, as grounds for the rejection, the following is noted:

- 1) it is acknowledged that the primary citation of Sasse et al. “does not teach the linker of PEGylation of the molecule”
- 2) the position is taken that without any support from the cited documents: “in order to couple the PEG to other molecules the PEG is activated via introducing a linker between the active moiety and PEG. When such an activated PEG is used in the formation of a conjugate, it is obvious to obtain a linker or spacer arm between the molecule of interest and PEG ....”
- 3) Greenwald is cited for “conjugates of drugs with higher molecular weight PEG(>20,000d) improve the solubility and half-life of the drug in mouse model ....”

The rejection is traversed.

As understood, the instant rejection is based on the position that Greenwald renders any PEG-conjugate compound obvious.

Respectfully, that position does not withstand scrutiny.

Indeed, Greenwald mentions nothing of tubulysin compounds. Thus, Greenwald clearly fails to mention or otherwise suggest any type of PEG conjugates of tubulysin compounds. In the Office Action, it was specifically acknowledged that the primary citation of Sasse et al. does not disclose conjugate compounds of any type.

Such rejection is clearly not proper. See, for example, Section 2143.03 of the Manual of Patent Examining Procedure (“To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.”).

The cited documents also do not disclose *inter alia* a group V as Applicants disclose and claim. See Applicants’ claims 16 through 20, among others.

In the Office Action, it is stated that “it is obvious to obtain a linker or spacer arm between the molecule of interest and PEG”, although no disclosure from the prior art is cited to support that position.

Respectfully, such an unsupported allegation of obviousness can not be relied on. See MPEP Section 2143.03, discussed above.

In view thereof, reconsideration and withdrawal of the rejection are requested.

Claims 7-10 and 12-17 stand rejected under 35 U.S.C. 112, first paragraph, although no evidence has been cited to substantiate why the present case might be non-enabling. The rejection is traversed.

The present application fully satisfies the rejection of 35 U.S.C. 112, including the make and use requirements of Section 112, first paragraph.

For instance, tubulysin compounds are disclosed at page 1 of the application. Linkers and polymers are disclosed in detail at page 7. At pages 11 and 12 of the application, specific examples are detailed.

Clearly based on such extensive disclosure as the present application, the skilled worker would have been able to make compounds of the invention.

Therapeutic uses of compounds of are detailed for instance at page 10 of the application. At page 1 of the application, therapeutic activity of tubulysin compounds are disclosed.

Moreover, no substantiating reasons have been advanced as to why one skilled in the art could not make and use the claimed invention. Indeed, the discussion above makes clear that one skilled in the art could readily practice the claimed invention in view of Applicants' disclosure.

Respectfully, such a rejection, lacking any supporting evidence or other substantiating grounds is simply not proper. Thus, for example, MPEP §2164.04 states the following (quoting *In re Marzocchi*, 169 USPQ 367):

[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

In view thereof, reconsideration and withdrawal of the rejection are requested.

Claims 7-10 and 12-17 were rejected under 35 U.S.C. 112, second paragraph. As grounds for the rejection, it is stated that the term "biomolecule" is indefinite. The rejection is traversed.

The skilled worker readily understands the term "biomolecule," particularly when considered in light of the supporting specification, as is proper. Thus, for instance, the term "biomolecule" is discussed in detail at page 7 of the application.

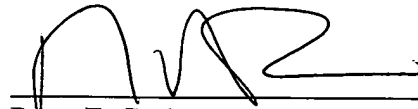
Attention is further directed to the Manual of Patent Examining Procedure at Section 2173.02, which states in part:

When the examiner is satisfied that patentable subject matter is disclosed, and it is apparent to the examiner that the claims are directed to such patentable subject matter, he or she should allow the claims which define the patentable subject with a reasonable degree of particularity and definiteness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire.

In view thereof, reconsideration and withdrawal of the rejection are requested.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,



Peter F. Corless

Registration No. 33,860  
EDWARDS ANGELL PALMER & DODGE LLP  
P.O. Box 55874  
Boston, Massachusetts 02205  
Tel. No. (617) 517-5564  
Customer No. 21,874